

An Evaluation of the Mutagenicity of Coke Oven Emissions Using US EPA's 2005 Supplemental Guidance for Assessing Cancer Susceptibility from Early-Life Exposure to Carcinogens

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Coke oven emissions are known to be carcinogenic to humans based on sufficient evidence of carcinogenicity that indicates a causal relationship between exposure and cancer in humans. The US EPA's Integrated Risk Information System (IRIS) health assessment for coke oven emissions (1989) utilizes a low-dose linear extrapolation to estimate the cancer risk. The US EPA has recently published Supplemental Guidance for Assessing Cancer Susceptibility from Early-Life Exposure to Carcinogens. This guidance recommends the use of an age-dependent adjustment factor for carcinogenic potency in which there are no early-life studies, but in which the available information is sufficient to establish a mutagenic mode of action for carcinogenesis. A review of the available mutagenicity data for coke oven emissions was performed to evaluate whether coke oven emissions are carcinogenic through a mutagenic mode of action. *In vitro* data suggest that coke oven emissions cause mutations in Salmonella test strains and mammalian cells in culture. Coke oven emissions also induce chromosomal damage in peripheral blood lymphocytes of exposed workers. Exposure to coke oven emissions causes sister chromatid exchanges, DNA adducts, micronucleus formation, and both single- and double-strand breaks in DNA. The role of polymorphisms has been considered; moderate support exists for an association between mutagenicity-related endpoints and polymorphisms in Phase I and Phase II metabolic enzymes. The available *in vitro* and *in vivo* genotoxicity and mutagenicity studies indicate coke oven emissions are carcinogenic to humans and operate through a mutagenic mode of action. Therefore, the use of an age-dependent adjustment factor for early-life exposure to coke oven emissions is warranted.

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